

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
29 December 2004 (29.12.2004)

PCT

(10) International Publication Number
WO 2004/112824 A1

- (51) International Patent Classification⁷: **A61K 38/17**, A61P 1/16
- (21) International Application Number: PCT/EP2004/006633
- (22) International Filing Date: 18 June 2004 (18.06.2004)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:
03291487.1 18 June 2003 (18.06.2003) EP
- (71) Applicant (for all designated States except US): **INSERM (INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE)** [FR/FR]; 101, rue de Tolbiac, F-75654 Paris Cedex 13 (FR).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): **CHRISTA, Laurence** [FR/FR]; 22, rue Armand Millet, F-92340 Bourg la Reine (FR). **BRECHOT, Christian** [FR/FR]; 35, boulevard Pasteur, F-75015 Paris (FR). **SIMON-GAGE-SOUF-FLOT, Marie-Thérèse** [FR/FR]; 37, rue Anatole France, F-92370 Chaville (FR). **PAULOIN, Alain** [FR/FR]; 16, Villa Astrid, 78960 Voisin-le-Bretonneux (FR). **TRAL-HAO, J. Guilherme** [PT/PT]; Av. Prof Elisio de Moura 397 1°C, P-3030 Coimbra (PT).
- (81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
- (84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

- with international search report
- with amended claims

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: **HIP/PAP POLYPEPTIDE COMPOSITION FOR USE IN LIVER REGENERATION AND FOR THE PREVENTION OF LIVER FAILURE**

(57) Abstract: This invention is based on the experimental finding that HIP/PAP has mitogenic and antiapoptotic effects in vitro on hepatocytes in primary culture. Moreover, HIP/PAP is a mitogenic and anti-apoptotic molecule for hepatocytes, *in vivo*, during liver failure and liver regeneration. The present invention is also based on the experimental finding that HIP/PAP administration has no adverse effects in mammals. This invention concerns a pharmaceutical composition for stimulating liver regeneration *in vivo* including after chronic/acute liver failure, comprising an effective amount of a polypeptide comprising an amino acid sequence having 90% amino acid identity with the polypeptide consisting of the amino acid sequence starting at the amino acid residue (36) and ending at the amino acid residue (175) of sequence SEQ ID N°1, in combination with at least one physiologically acceptable excipient.

WO 2004/112824 A1